Pregnant Pause

Does Maternal PBDE Exposure Extend Time to Pregnancy?

Animal studies indicate polybrominated diphenyl ethers (PBDEs) are endocrine disruptors, potentially affecting the role of thyroid hormones in regulating the reproductive cycle and fertility. The compounds also have been associated with delayed puberty and altered estradiol levels in female animals. Very little is known about the potential effects of PBDEs on human reproductive health, though, and a new study is the first to characterize a specific concern—a relationship between PBDE blood concentrations and a delay in achieving pregnancy [***EHP* 118:699–704; Harley et al.**].

PBDEs are used as flame retardants in furniture, carpeting, textiles, electronics, and plastics. Commercial mixtures of PBDEs contain a variety of congeners, or chemical variations. Data collected by the Centers for Disease Control and Prevention suggest 97% of Americans may have detectable levels of PBDEs in their blood.

The current study included 223 pregnant women enrolled in the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS), a longitudinal birth cohort study focused on environmental exposures and reproductive health in California's Salinas Valley. Upon enrollment, the women reported their reproductive history, previous use of contraception and fertility medication, whether the pregnancy was planned, and how long it took to become pregnant after stopping contraception.

Blood samples collected around 26 weeks of pregnancy were analyzed for 10 PBDE congeners. Statistical analyses focused on those most commonly found: BDE-47, BDE-99, BDE-100, and BDE-153. BDE-100 and BDE-153 were the most strongly associated with longer time to pregnancy. For each month, the likelihood of becoming pregnant was 40% or 50% lower with a 10-fold increase in concentration of BDE-100 or -153, respectively. With a 10-fold increase in the total of all 4 congeners, there was a 30% decrease in the odds of pregnancy each month.

The study relied on self-reported time to pregnancy, which is subject to a number of biases. In addition, the study's findings are limited to 4 PBDE congeners and may not extend to a broader population. Consequently, further research incorporating more congeners and a more representative population is needed. However, given the likelihood of PBDE exposure in the general population, even a small effect of these chemicals on fertility may affect a large number of individuals.

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Cancer Collusion?

Dietary Fat May Modify Dioxin-Induced Mammary Cancer Risk

Some human and animal studies have linked early-life exposure to the endocrine-disrupting chemical 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) with an increased susceptibility to breast cancer. Dietary fat has been posited as another potential risk factor for breast cancer, possibly acting through the estrogen pathway. A new animal study suggests a high-fat diet may alter estrogen metabolism, thereby modifying the effects of maternal exposure to TCDD and increasing mammary cancer risk in the next generation [***EHP* 118:596–601; La Merrill et al.**].

One group of pregnant female FVB/NJ mice (a TCDD-responsive mouse strain) received an olive oil/toluene blend with TCDD; another received an equivalent volume of olive oil/toluene without TCDD. Their female offspring were randomly assigned to either a low-fat or high-fat diet and exposed to the carcinogen 7,12-dimethyl-benz[*a*]anthracene (DMBA) at days 35, 49, and 63 after birth in order to initiate mammary tumors. A second cohort of female offspring was treated identically until either day 35 or 49, when morphologic and molecular analyses of their mammary glands were performed.

Maternal TCDD exposure was associated with a doubling of mammary tumor incidence only in offspring fed the high-fat diet. In contrast, no mammary tumors arose in mice exposed to TCDD *in utero* and fed the low-fat diet. Whereas one-third of TCDD-unexposed litters fed a high-fat diet had DMBA-induced mammary lesions, every litter exposed to both TCDD and a high-fat diet developed mammary lesions.

Previous animal studies had shown that prenatal exposure to TCDD alters mammary gland differentiation and increases susceptibility to mammary cancer. However, this is the first to show that TCDD may interact with a high-fat diet during pregnancy and early life. The researchers propose that a high-fat diet may boost sensitivity to maternal TCDD exposure by altering estrogen metabolism.

The new findings highlight a possible mechanism that may explain epidemiologic data separately linking early-life TCDD exposure and high-fat diets to increased breast cancer risk in humans. In the present study, TCDD exposure *in utero* combined with a high-fat diet was also associated with increased expression of *Cyp1b1* and decreased expression of *Comt* in mammary tissue. Human studies have suggested that diminished *COMT* expression and increased *CYP1B1* expression are associated with increased risk of breast cancer and other estrogen-responsive cancers, perhaps by increasing levels of estrogen metabolites that can contribute to carcinogenesis by damaging DNA. They also note that obesity may affect breast cancer risk because TCDD persists in adipose tissue, including that in the breast.

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